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ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND MODERATE TO SEVERE PERIODONTITIS IN ADULTS: A RANDOMISED CLINICAL TRIAL

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Abstract -To find whether any relationship exist between Periodontitis and Rheumatoid arthritis.
Material and method- A total of 80 subjects between the ages 20-70 years were included in the study,
which is done in three parts.
PART A: includes selection of 80 patients with Chronic Periodontitis which are diagnosed with RA by the Rheumatologist.
PART B: includes evaluation of severity of Periodontitis in RA patients selected in Part A, using the Clinical Attachment Level data into mild, moderate and severe periodontitis.
PART C: includes segregation of 10 patients, from total patients, with severe Periodontitis using CAL data and severe RA as diagnosed by the Rheumatologist. These patients will undergo Phase I periodontal therapy.
Laboratory parameters for RA: Haemogram, ESR, CRP level, RA factor and Anti CCP antibody.
Result -Prevalence of moderate or severe periodontitis was higher in RA than in NRA group. Periodontal structural damage represented by clinical attachment level was more in RA patients. Mostly females (63.75%) suffered with rheumatoid arthritis as compared to males (36.25%). Female to male ratio was 1.75:1. The mean value of PI, SBI, PPD, CAL, and tooth mobility gradually increases with the increase in the age of patients with Chronic Periodontitis. Out of 80 patients, 88.75% cases presented with swelling in joints followed by 80% with arthritis joints, 78.75% with stiffness and only 8.75% patients have rheumatoid nodules. Out of 80 patients, 10 patients with severe rheumatoid arthritis and severe periodontitis. The comparison of mean values, in 10 patients with severe periodontitis and severe RA, for PI, SBI, PPD, CAL and tooth mobility at baseline and after 4 weeks of phase I periodontal therapy was statistically significant (P<0.0001*** each).
Conclusion-Individuals who are suffering from RA are also very likely to suffer from moderate to severe periodontitis.

Keywords-Periodontitis, Rheumatoid arthritis, RA

Introduction:

Periodontitis and Rheumatoid arthritis (RA) are two common chronic inflammatory diseases sharing a similar host-mediated pathogenesis[1] . Periodontitis is characterized by soft and hard tissue

destruction around the teeth, ultimately leading to tooth loss[2] , while RA is characterized by destruction of cartilage and bone in the joints, mediated by similar bone-resorptive cytokines and proteinases[1,3].

Both diseases lead to significant morbidity, with periodontitis ultimately leading to tooth loss and loss of masticatory function, and RA leading to loss of joint function and loss of mobility. Growth of scientific evidence suggests an exquisite association between oral infection and systemic diseases. However, of growing interest is the effect of periodontal diseases on numerous systemic diseases or conditions like rheumatoid arthritis, cardiovascular disease, diabetes, pre-term low birth weight babies, cerebrovascular disease. Of growing interest is the evidence that suggest periodontal disease as an independent risk-factor for a number of significant systemic diseases so much so that they have brought a shift in the rationale about casuality and the directionality of oral and systemic associations.

This paradigm shift is encapsulated by the new term Periodontal Medicine. The term Periodontal Medicine, as first suggested by Offenbacher (1996), can be viewed as a broad term that defines a rapidly emerging branch of Periodontology focusing on the wealth of new data establishing a strong relationship between periodontal health or disease and systemic health or disease. Oral infection can either cause or aggravate many diseases[5] .Thought etiologies of periodontitis and rheumatoid arthritis (RA) are separate, but their underlying pathological processes are sufficient to warrant consideration of hypothesis that individual at risk of developing RA may also be at the risk of developing periodontitis and vice versa[4] . Periodontitis disease is an all- encompassing term relating to the destruction of the hard and soft tissues surrounding the teeth[6] . Periodontitis is initiated by pathogenic biofilm that accumulates around the gingival margin and in gingival crevice[7]. RA is a chronic, immune- mediated inflammatory disease that is characterized by synovial inflammation and progressive destruction of cartilage and bone that often results in structural damage, disability and loss of joint function. RA is associated with significant morbidity and an increased risk of mortality (premature death)[8]. The chronic inflammation of periodontal disease (PD) with the constant release of inflammatory mediators may be a risk factor for the development of systemic inflammatory disease[9].

The human mouth is the second largest bacterial community of the body, after the lower gastrointestinal tract. Scientists have identified over 700 oral cavity bacterial species[11]. The oral microbiota is involved in the etiology of PD, and it may be a contributory factor in the etiopathogenesis of some chronic inflammatory diseases, such as RA[10]. Periodontal pathogens can enter the systemic circulation as a result of bacteremia after brushing the teeth, chewing, and after dental treatment[12,13] . Several studies suggested that a higher prevalence of severe periodontitis and tooth loss caused by PD correlates with RA activity[3,18,24,25,26]. It is now generally accepted that chronic periodontitis is initiated by the colonisation of dental plaque by several periopathogenic bacteria: Porphyromonas gingivalis, Prevotella intermedia, Treponema denticola and Tannerella forsythia[7]. The DNA of these bacteria has been detected in the synovial fluid of patients with RA[14,15] . The Porphyromonas gingivalis, the most common pathogen of PD, is of particular peptides, human α-enolase peptides and fibrinogen[16]. Therefore, PAD is the major candidate for explaining the possibility that PD is an etiogenic factor for RA[17].

Periodontitis is a common disease worldwide that has a primarily bacterial etiology and is characterized by a dysregulation of the host inflammatory response, eventually resulting in soft and hard tissue destruction[18,20]. According to various epidemiological studies, periodontal diseases are one of the most prevalent oral diseases affecting more than 50% of total Indian population[21]. Periodontitis has remarkably similar pathobiology to rheumatoid arthritis (RA). Rheumatoid arthritis (RA) is a systemic inflammatory disorder with a prevalence of 0.5% to 1.0% in Western populations; it affects women about three times more often than men[22]. More recently it has been reported that patients with periodontitis are 4 times more likely to have self reported history of rheumatoid arthritis[6]. The relationship between rheumatoid arthritis (RA) and the progression of inflammatory conditions elsewhere in the body, such as periodontitis, is controversial. While a

number of studies have presented conflicting results regarding a relationship between periodontitis and RA, there has been recent reports' suggesting a significant association between these two common chronic inflammatory conditions[23]. In light of these reports, there is a need for further investigations to determine whether the severity of RA and the severity of periodontitis are interrelated. Hence, development of both diseases brings considerable consequences for public health and for the quality of life of affected individuals. To test whether a relationship exist between Periodontitis and RA, this study was conducted.

Material and Method-

A total of 80 subjects between the ages 20-70 years were included in the study, which is done in three parts.

Patients (20-70 years old) diagnosed with RA by the Rheumatologist (Dr. Renu Saigal, Jaipur, Rajasthan). The criteria used by the Rheumatologist to diagnose the patient with RA and severity of RA is as follows:

Rheumatoid arthritis examination: Morning stiffness, Arthritis of three or more joint areas,Arthritis of hand joints, Symmetric arthritis, Rheumatoid nodules, Serum rheumatoid factor, Radiographic changes

A person was diagnosed for RA if at least four out of these seven criteria were met for at least ≥ six weeks.

Clinical assessment(s) to determine the extent of severity of RA-Duration of early morning stiffness: It was measured in minutes from the time of awakening to the time sensation began to wear off.

Grip Strength: It was measured with a mercury sphygmomanometer.

Walking time: Time in seconds required to walk straight to a distance of 50 feet was taken.

Pain: was assessed by the patient on visual analog scale (VAS) of 10 cm.

Tender/swollen joint count: It was assessed in 58 joints

Laboratory parameters for RA:

Haemogram, ESR, CRP level, RA factor and Anti CCP antibody.

Study design: The study is conducted in three parts.

PART A: includes selection of 80 patients with Chronic Periodontitis which are diagnosed with RA by the Rheumatologist according to the criteria as discussed previously.

PART B: includes evaluation of severity of Periodontitis in RA patients selected in Part A, using the Clinical Attachment Level data into mild, moderate and severe periodontitis.

PART C: includes segregation of 10 patients, from total patients, with severe Periodontitis using CAL data and severe RA as diagnosed by the Rheumatologist. These patients will undergo Phase I periodontal therapy.

Baseline recording of clinical parameters for periodontal status:- Plaque Index (Sillness & Loe 1964)**,** Sulcus Bleeding Index (Muhlemann H.R. and Son S. 1971)**,** Probing Pocket Depth**,** Clinical Attachment levels (using UNC-15 probe)**,** Tooth mobility index (Miller's classification)

Radiological parameters for periodontal status:- Orthopantomogram

Phase I periodontal therapy includes the following: 10 patients selected in Part C with severe Periodontitis and severe RA will be subjected to Phase I periodontal therapy- scaling and root planing and instructions for plaque-control were given.

Re-evaluation after Phase I periodontal therapy (after 4 weeks): All the gingival and periodontal indices mentioned previously in the study and RA parameters (clinical, laboratory and radiological as assessed by the Rheumatologist) were re-evaluated 4 weeks after completion of Phase I periodontal therapy.

Method of statistical analysis used in this study: Chi-square test**,** Formula Xa, b 2 =∑(O-E)2 /E**,** Unpaired t – test**,** Formula t=X1 –X2 /√S2 (1/n1 +1/n2)**,** Paired t - test =Mean observed difference/Standard Error (SE) of observed difference.

Result-In this study, maximum number of cases (28.75%) were seen in 61-70 years of age group followed by 51-60 years (26.25%) and 25% in 41-50 years of age(Table 1).

Mostly females (63.75%) suffered with rheumatoid arthritis as compared to males (36.25%). Female to male ratio was 1.75:1. (Table 2). In our study, the mean value of PI, SBI, PPD, CAL and tooth mobility gradually increases with increase in the age of patients with Chronic Periodontitis. (Table 3). This study pointed out that 88.75% cases presented with swelling in joints followed by 80% with arthritis joint, 78.75% with stiffness and only 8.75% patients have rheumatoid nodules. (Table 4).The 61-70 years of age group, presented with more stiffness of joints, swelling, rheumatoid nodules and arthritis joint. (Table 5)

The mean value of ESR, RBC count, MPV, WBC, RA factor, Anti-CCP and CRP were calculated for all the included cases. The mean value of ESR, RBC count, MPV, WBC, RA factor, Anti-CCP, and CRP were 14.66±7.741, 3.944±0.5624, 8.504±1.425, 7.290±1.823, 9.656±2.376, 6.754±4.763 and 4.531±2.555 respectively. (Table 6) This study indicated that the mean value of ESR, RBC count, MPV, WBC, RA factor, ANTI-CCP and CRP were more in 61-70 years of age group as compared to 20-30 years of age group with chronic periodontitis (18.43±11.7 v/s 12.40±4.15, 4.18±0.75 v/s 3.54±0.23, 9.12±1.95 v/s 8.44±0.56, 7.61±2.15 v/s 7.04±2.09, 10.19±2.57 v/s 7.920±0.9834, 10.88±5.13 v/s 5.0±2.55 and 8.72±3.252 v/s 4.2±0.836 respectively). (Table 7). It was seen in our study that, out of 80 patients, 10 patients with severe Periodontitis and severe RA were evaluated at base line. The mean age of these 10 patients was 63.40 years and male to female ratio was 2:3. The mean value of clinical profile, rheumatoid parameters and biochemical profile was more at baseline for these 10 patients. (Table 8).The mean value of clinical profile and biochemical profile of 10 patients with severe periodontitis and severe RA was less after 4 weeks of Phase I periodontal therapy. (Table 9)

Table 1: Age wise distribution of cases

Age Group (yrs)	Number	Percentage
21-30 yrs	5	6.25%
31-40 yrs	11	13.75%
41-50 yrs	20	25%
51-60 yrs	21	26.25%
61-70yrs	23	28.75%
Total	80	100%

Table 2: Gender wise distribution of cases

Gender	Number	Percentage
Male	29	36.25%
Female	51	63.75%
Total	80	100%

Table 3: Periodontal clinical profile of all the cases according to the age group

Age group (yrs)	PI	SBI	PPD	CAL	Mobility
20-30 yrs	2.4±1.08	2.32±0.76	5.1±0.36	2.16±1.14	0.98±0.49
31-40 yrs	2.16±0.98	2.36±0.91	4.47±0.70	2.82±1.03	1.02±0.46
41-50 yrs	2.165±1.02	2.42±0.75	4.33±0.99	2.34±1.11	1.16±0.39
51-60 yrs	2.86±1.31	2.34±1.14	4.98±1.12	3.01±2.07	1.24±0.45
61-70 yrs	3.20±1.09	3.15±1.38	5.38±1.58	3.51±2.59	1.28±0.49

Table 4: Rheumatoid parameters of all the included cases

Rheumatoid parameters	Number	Percentage
Stiffness	63	78.75%
Swelling	71	88.75%
Rheumatoid nodule	7	8.75%
Arthritis Joint	64	80%

Table 5: Rheumatoid parameters of total cases according to the age group

Age group (yrs)	Stiffness	Swelling	Rheumatoid Nodules	Arthritis joint
20-30 yrs	5	5	0	5
31-40 yrs	8	11	0	8
41-50 yrs	16	17	1	15
51-60 yrs	19	17	1	17
61-70 yrs	23	21	5	19

Table 6: Biochemical profile of all included RA cases

Biochemical Profile	Mean	SD
ESR	14.66	7.741
RBC count	3.944	0.5624
MPV	8.504	1.425
WBC	7.290	1.823
RA Factor	9.656	2.376
ANTI-CCP	6.754	4.763
CRP	4.531	2.555

Table 7: Clinical profile of all RA cases according to the age group

Biochemical profile	20-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs
ESR	12.40±4.15	12.64±3.32	11.40±3.33	15.24±5.80	18.43±11.7
RBC count	3.54±0.23	3.71±0.34	3.8±0.35	4.02±0.52	4.18±0.75
MPV	8.44±0.56	8.24±1.06	8.3±1.37	8.19±0.86	9.12±1.95
WBC	7.04±2.09	6.82±1.67	7.16±1.61	7.36±1.73	7.61±2.15
RA Factor	7.920±0.9834	8.682±1.206	9.26±1.596	10.68±1.567	10.19±2.57
ANTI-CCP	5.0±2.55	5.90±1.446	5.65±1.63	8.810±4.131	10.88±5.13
CRP	4.2±0.836	3.64±1.36	4.1±1.33	4.33±1.6	8.72±3.252

Table 8: Profile of 10 patients with severe Periodontitis and severe RA at baseline

Demographic profile	
Mean age	63.40±5.967
Male:Female	2:3
Clinical Profile	
Plaque Index (PI)	4.380±0.5029
Sulcular Bleeding Index (SBI)	4.900±0.2539
Probing Pocket Depth (PPD)	7.250±0.7184
Clinical Attachment Loss (CAL)	7.140±0.8972
Mobility	1.610±0.3123
Rheumatoid parameters	
Stiffness	9
Swelling	10
Rheumatoid nodule	3
Arthritis Joint	10

Biochemical profile	
ESR	31±10.31
RBC count	4.98±0.6743
MPV	10.35±1.907
WBC	8.390±2.369
RA Factor	13.80±1.130
ANTI-CCP	20.09±1.300
CRP	9.550±4.098

Table 9: Profile of 10 patients with severe periodontitis and severe RA after 4 weeks of Phase I periodontal therapy

Clinical Profile	
Plaque Index (PI)	1.320±0.2898
Sulcular Bleeding Index (SBI)	2.140±0.3373
Probing Pocket Depth (PPD)	4.140±0.8316
Clinical Attachment Loss (CAL)	4.780±0.5350
Mobility	0.9890±0.1362
Biochemical profile	
ESR	17.0±2.667
RBC count	5.421±0.4511
MPV	11.06±1.247
WBC	10.15±1.647
RA Factor	11.80±1.248
ANTI-CCP	17.66±1.316
CRP	6.600±1.614

Table 10: Comparison of mean in 10 patients with severe periodontitis and severe RA at baseline and after 4 weeks of Phase I periodontal therapy

	Baseline	**After 4 weeks of SRP**	**P-value**
Clinical Profile			
Plaque Index (PI)	4.380±0.5029	1.320±0.2898	<0.0001***
Sulcular Bleeding Index (SBI)	4.900±0.2539	2.140±0.3373	<0.0001***
Probing Pocket Depth (PPD)	7.250±0.7184	4.140±0.8316	<0.0001***
Clinical Attachment Loss (CAL)	7.140±0.8972	4.780±0.5350	<0.0001***
Mobility	1.610±0.3123	0.9890±0.1362	<0.0001***
Biochemical profile			
ESR	31±10.31	17.0±2.667	0.0006***
RBC count	4.98±0.6743	5.421±0.4511	0.1057 NS
MPV	10.35±1.907	11.06±1.247	0.3375 NS
WBC	8.390±2.369	10.15±1.647	0.0696 NS
RA Factor	13.80±1.130	11.80±1.248	0.2748 NS
ANTI-CCP	20.09±1.300	17.66±1.316	0.0006***
CRP	9.550±4.098	6.600±1.614	0.0483*

Discussion- Periodontitis and rheumatoid arthritis (RA) are both common chronic inflammatory diseases sharing almost similar host-mediated pathogenesis[1]. Both diseases lead to significant morbidity, with periodontitis ultimately leading to tooth loss and loss of masticatory function, and RA leading to loss of joint function and loss of movement. Thought etiologies of periodontitis and rheumatoid arthritis (RA) are separate, their underlying pathological processes are sufficient to warrant consideration of hypothesis that individual at risk of developing RA may also be at the risk

of developing periodontitis and vice versa[4]. Several studies suggested that a higher prevalence of severe periodontitis and tooth loss caused by PD correlates with RA activity. In light of these reports, there is a need for further investigations to determine whether the severity of RA and the severity of periodontitis are interrelated. Hence, development of both diseases brings considerable consequences for public health and for the quality of life of affected individuals. To test whether a relationship exist between Periodontitis and RA, this study was conducted.

The majority of clinical and epidemiological studies indicate that patients with RA have increased prevalence of periodontitis and tooth loss[15,23]. In our study, we found that maximum number of cases (28.75%) were seen in 61-70 years of age group followed by 51-60 years (26.25%) and 25% in 41-50 years of age. The mean age of patient was 62 years and the disease RA most commonly occurred in female patients which has reflected the epidemiology of disease. The finding, that more females (64%) were affected by RA is consistent with findings by (Mercado et al., 2001)[23] in which (74.6%) female were affected by the disease. In this study, it was found that the mean value of PI, SBI, PPD, CAL and tooth mobility gradually increases with increase in the age of patients with Chronic periodontitis. This was in accordance with the study of Kabayashi et al. in which 100 patients with RA and 100 patients without RA were included. The group with RA had 3.3 more teeth missing than the control group. Kasser et al. , Garib and Qaradaxi and Joseph et al. , got similar results. All this indicates that the extent of tooth loss is greater in patients with RA than in patients without RA which is also seen in our study. Moreover, a review article by Kaur et al. indicated that severe periodontitis including greater CAL and increased tooth loss is associated with RA, although the authors concluded that larger population-based studies were needed to confirm this link .Our study pointed that the mean value of ESR, RBC count, MPV, WBC, RA factor, ANTI-CCP and CRP were more in 61-70 years of age group as compared to 21-30 years of age in chronic periodontitis individuals ,which is in accordance with the study by Khare N et al, 2016.

Out of 80 patients in this study, 10 patients with severe rheumatoid arthritis and severe Periodontitis were evaluated at baseline and after 4 weeks of phase I periodontal therapy. The mean age of these 10 patients was 63.40 years and male to female ratio was 2:3 which is in accordance with study by Mercado et al, 2001[23] . The comparison of mean of PI, SBI, PPD, CAL and tooth mobility of 10 patients with severe periodontitis and severe RA at baseline from that of after 4 weeks of phase I periodontal therapy, was statistically significant (P<0.0001*** each). The mean value of ESR, ANTI-CCP and CRP were also statistically significant (P=0.0006***, P=0.0006*** & P=0.0483* respectively) for these 10 patients but, the mean of RBC count, MPV, WBC and RA factor was not statistically significant. Ribeiro J et al (2005) suggested that periodontal treatment with SRP might have an effect on the ESR reduction. Al-Katma MK et al (2007) concluded that control of periodontal infection and gingival inflammation by scaling/root planing and plaque control in subjects with periodontal disease may reduce the severity of RA. Joseph R et al (2013) found statistically significant difference in GI, OHI-S, PPD, CAL, ESR and CRP levels between cases (RA group) and controls (NRA group) (P < 0.05) showing resemblance with our study. Mercado FB et al (2001)[23] found that no differences were noted for the plaque and bleeding indices between the control and rheumatoid arthritis groups. The rheumatoid arthritis group did, however, have more missing teeth than the control group and a higher percentage of these subjects had deeper PPD. When the percentage of bone loss was compared with various indicators of rheumatoid arthritis disease activity, it was found that swollen joints, health assessment questionnaire scores, levels of C-reactive protein, and erythrocyte sedimentation rate were the principal parameters which could be associated with periodontal bone loss. Furthermore, in an Australian population (including 65 RA cases and 65 controls), increased periodontal bone loss and deeper pockets were associated with indicators of RA disease activity, such as higher number of swollen joints, and levels of CRP and ESR in patients with RA. Conversely, there are also studies reporting no association between levels of ESR or CRP and Periodontitis. A meta-analysis performed in 2013 by Kaur et al. reported no statistical difference in ESR titers, and only low level of evidence for elevated CRP and the association with periodontitis in RA subjects. The conflicting reports on the relationship between

periodontitis and RA, discussed in this study, may depend on ethnic differences between study populations and/or substantial differences in disease classification criteria for periodontitis. In 2013, Linden et al. concluded that studies do not provide support for a link between periodontitis and RA since very few studies meet a stringent threshold for Periodontitis. Moreover, in a recently published review by Chapple et al. the authors state that even though patients with RA seem to have an increased prevalence of periodontitis, they deemed the certainty of this association as low.

Conclusion- Our findings suggest large population-based studies will be needed to define the role of periodontitis in RA disease susceptibility. However, our findings suggest greater attention to periodontal care among the RA patients. The prevention, treatment and maintenance of periodontitis patients need to be advocated by the Periodontist. Hence, it is suggested to develop new host modifying medications that can reduce the inflammatory component of the disease. However, studies with a larger sample size, longer follow-up are necessary to support and confirm the findings.

References-

1. Rosenstein ED, Greenwald RA, Kushner LJ, Weissmann G. Hypothesis: the humoral immune response to oral bacteria provides a stimulus for the development of rheumatoid arthritis. Inflammation. 2004;28:311–8.
2. Kornman KS. Mapping the pathogenesis of periodontitis: a new look. J Periodontol. 2008;79:1560–8.
3. Schett G, Teitelbaum SL. Osteoclasts and arthritis. J Bone Miner Res. 2009; 24:1142–6.
4. Ranade SB, and Doiphode S. Is there relationship between periodontitis and rheumatoid arthritis.JIndiaSocPeriodontal. 2012; 16(1):22-27.
5. Shafer William G., Hine Maynard K., Levy Barnet M. Spread of oral infection. A textbook of oral pathology. (4 thed). 1993: 511- 27.chapter 9.
6. Mercado F, Marshall RI, Kelstov AC, Bartold PM. Is there relationship between rheumatoid arthritis and periodontal diseases. J Clin Periodontol .2000; 27:267-72.
7. Socaransky, S.S. et al. Microbial complexes in subgingival plaque. J. Clin. Periodontol.1998; 25: 134-144.
8. Gabriel, S.E. et al. Mortality in rheumatoid arthritis. Have we made an impact in 4 decades? J. Rheumatol.1999; 26:2529-2533.
9. Linden GJ, Lyons A, Scannapieco FA. Periodontal systemic associations: Review of the evidence. J Clin Periodontol. 2013; 40: 8-19.
10. Loyola-Rodriguez JP, Martinez-Martinez RE, Abud-Mendoza C, PatiñoMarin N, Seymour GJ. Rheumatoid arthritis and the role of oral bacteria. J Oral Microbiol. 2010; 21: 2.
11. Yeoh N, Burton JP, Suppiah P, Reid G, Stebbings S. The role of the microbiome in rheumatic diseases. Curr Rheumatol Rep. 2013; 15: 314.
12. Forner L, Larsen T, Kilian M, Holmstrup P. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. J Clin Periodontol. 2006; 33: 401-417.
13. Kinane DF, Riggio MP, Walker KF, MacKenzie D, Shearer B. Bacteraemia following periodontal procedures. J Clin Periodontol. 2005; 32: 708- 713.
14. Scher JU, Ubeda C, Equinda M, Khanin R, Buischi Y, Viale A, et al. Periodontal disease and the oral microbiota in new-onset rheumatoid arthritis. Arthritis Rheum. 2012; 64: 3083-3094.
15. De Smit MD, Westra J, Vissink A, van der Meer B, Brouwer E, van Winkelhoff AJ. Periodontitis in established rheumatoid arthritis patients: A cross-sectional clinical, microbiological and serological study. Arthritis Res Ther. 2012; 14: 222-228.
16. Wegner N, Wait R, Sroka A, Eick S, Nguyen K-A, Lundberg K, et al. Peptidylarginine deiminase from Porphyromonas gingivalis citrullinates human fibrinogen and a-enolase: Implications for autoimmunity in rheumatoid arthritis. Arthritis Rheum. 2010; 62: 2662-2772.

17. Adriano-Arajo VM, Matos-Melo I, Lima V. Relationship between periodontitis and rheumatoid arthritis: Review of the literature. Mediators Inflamm. 2015; 1: 1-15.
18. Bartold PM, Marshall RI, Haynes DR. Periodontitis and rheumatoid arthritis: a review. J. Periodontol. 2005; 76(Suppl. 11): 2066–2074.
19. de Pablo P, Chapple IL, Buckley CD, Dietrich T. Periodontitis in systemic rheumatic diseases. Nat. Rev. Rheumatol.2009; 5(4): 218–224.
20. Mercado FB, Marshall R, Bartold PM. Inter-relationship between rheumatoid arthritis and periodontal disease. A review. J Clin Periodontol 2003; 30:761- 772.
21. Agarwal V, Khatri M, Singh G, Gupta G, Marya CM, Kumar V. Prevalence of Periodontal Diseases in India. J Oral Health Comm Dent 2010; 4(Spl):7-16.
22. Lee DM, Weinblatt ME. Rheumatoid arthritis. Lancet 2001; 358:903-911.
23. Mercado FB, Marshall RI, Klestov AC, Bartold PM. Relationship between rheumatoid arthritis and periodontitis. J Periodontol 2001; 72:779- 787.
24. Lang N, Lindhe J: Clinical Periodontology and Implant Dentistry 6th edn: John Wiley & Sons; 2015.
25. Pischon N, Pischon T, Kröger J, Gülmez E, Kleber BM, Bernimoulin JP, Landau H, Brinkmann PG, Schlattmann P, Zernicke J, Buttgereit F, Detert J. Association among rheumatoid arthritis, oral hygiene, and periodontitis. J Periodontol. 2008 Jun;79(6):979-86.
26. Seymour, G.J., Ford, P.J., Cullinan, M.P., et al. Relationship between periodontal infections and systemic disease. Clin Microbiol Infect 2007; 13: 3-10.